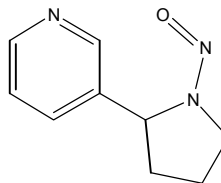


N-NITROSONORNICOTINE

CAS No. 16543-55-8

First Listed in the *Second Annual Report on Carcinogens*



CARCINOGENICITY

N-Nitrosornornicotine is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC V.17, 1978; IARC S.4, 1982; IARC V.37, 1985; IARC S.7, 1987). When administered in the drinking water, *N*-nitrosornornicotine induced esophageal carcinomas and papillomas and carcinomas of the nasal cavity in rats of both sexes, nasal cavity adenocarcinomas in female rats, and papillomas of the nasal cavity and trachea in hamsters of both sexes. When administered in the diet, *N*-nitrosornornicotine induced esthesioneuroepitheliomas and squamous cell carcinomas of the nasal cavity, and squamous cell carcinomas of the esophagus in male rats. When administered by subcutaneous injection, *N*-nitrosornornicotine induced olfactory neuroblastomas, rhabdomyosarcomas, esthesioneuroepitheliomas, squamous cell and anaplastic carcinomas, spindle cell sarcomas, and lung adenomas, in rats of both sexes and tracheal papillomas in hamsters of both sexes. Intraperitoneal injection of *N*-nitrosornornicotine induced multiple pulmonary adenomas in mice of both sexes, lung adenomas in female mice, and nasal cavity tumors and tracheal papillomas in male hamsters (IARC V.37, 1985).

There are no adequate data available to evaluate the carcinogenicity of *N*-nitrosornornicotine in humans.

PROPERTIES

N-Nitrosornornicotine is a yellow oily liquid at ambient room temperature. It is soluble in water. *N*-Nitroso compounds are readily degraded in the presence of ultra-violet or visible light. When heated to decomposition, it emits toxic fumes of nitrogen oxides (NO_x).

USE

N-Nitrosornornicotine reportedly does not have a commercial use but is used as a research chemical (IARC V.37, 1985).

PRODUCTION

There are no current production data available for *N*-nitrosornornicotine. The Chem Sources USA directory identified one supplier of *N*-nitrosornornicotine in 1986 (Chem Sources, 1986). *N*-Nitrosornornicotine may be synthesized in small quantities primarily for use in research (HEEP, 1980). No import or export data were available. There is no evidence that it has been manufactured commercially in the United States.

EXPOSURE

The primary routes of potential human exposure to *N*-nitrosornicotine are inhalation, ingestion, and dermal contact. Cigarette smokers, tobacco chewers, cancer researchers, and organic chemists appear to be at greatest risk of possible exposure to *N*-nitrosornicotine. *N*-Nitrosornicotine has been found in a variety of tobacco products (chewing tobacco, snuff, cigarettes, and cigars), in mainstream and sidestream smoke from cigars and cigarettes, in saliva of chewers of betel quid with tobacco, and in saliva of oral-snuff users. Some of the *N*-nitrosornicotine in saliva appears to be formed endogenously from nitrite in saliva and tobacco alkaloids. Thus, there is widespread exposure to *N*-nitrosornicotine among users of tobacco products and those exposed to sidestream smoke. *N*-Nitrosornicotine is reported to be produced by nitrosation of nicotine during the curing, ageing, processing, and smoking of tobacco. About half of the *N*-nitrosornicotine originates in the unburnt tobacco, whereas the remainder is formed during burning. *N*-Nitrosornicotine has been found in tobacco at concentrations of 0.2-130 mg/kg, in snuff products at 0.8-77 mg/kg, in chewing tobacco at 1.0-90.6 mg/kg, and in cigarette smoke at 0.1-3.7 µg/cigarette (IARC V.37, 1985).

N-Nitrosamines are frequently produced during rubber processing and may be present as contaminants in the final rubber products. Potential exposure depends on the ability of the nitrosamines to migrate from the product and enter the body. Significant levels of *N*-nitroso compounds have been identified in a number of materials including pesticides, cosmetics, cutting fluids, and fire resistant hydraulic fluids. The *N*-nitroso compounds found in these products were apparently formed in situ during storage or handling as the result of a reaction between amines present in the mixture and inorganic nitrite, which may have been added as a corrosion inhibitor (CHIP, 1978). In air it solely exists as a gas (half-life 13 hours) and in soil its adsorption is pH dependent. Adsorption is higher in acidic conditions than in basic soil.

REGULATIONS

EPA regulates *N*-nitrosornicotine under the Resource Conservation and Recovery Act (RCRA) and Superfund Amendments and Reauthorization Act (SARA). *N*-Nitrosornicotine is subject to reporting/recordkeeping requirements under RCRA and SARA. EPA solicited comments on the designation of a reportable quantity (RQ) for *N*-nitrosornicotine under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). OSHA regulates *N*-nitrosornicotine under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-109.